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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/944,849	08/31/2001	Brian J. Nickoloff	212583	4478

23460 7590 05/22/2003

LEYDIG VOIT & MAYER, LTD
TWO PRUDENTIAL PLAZA, SUITE 4900
180 NORTH STETSON AVENUE
CHICAGO, IL 60601-6780

EXAMINER	
KAUFMAN, CLAIRE M	

ART UNIT	PAPER NUMBER
1646	8

DATE MAILED: 05/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/944,849	NICKOLOFF ET AL.	
	Examiner	Art Unit	
	Claire M. Kaufman	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-53* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-5 and 14-17, drawn to a method of inducing differentiation of an epithelial cell by providing intracellularly a Notch agonist, classification dependent on structure of agonist, for example, classified in class 512, subclass 2.

II. Claims 1-4, 6-17, drawn to a method of inducing differentiation of an epithelial cell by providing extracellularly a Notch agonist, classification dependent on structure of agonist, for example, classified in class 512, subclass 2.

III. Claims 18-21 and 30-33, drawn to method of inducing formation of a barrier in epithelium by providing a Notch agonist intracellularly, classification dependent on structure of agonist, for example, classified in class 512, subclass 2.

IV. Claims 18, 19, 22-33, drawn to method of inducing formation of a barrier in epithelium by providing a Notch agonist extracellularly, classification dependent on structure of agonist, for example, classified in class 512, subclass 2.

V. Claims 34 and 35, drawn to method of producing differentiated epidermis by culturing epithelium in the presence of a Notch agonist, classified in class 435, subclass 371.

VI. Claims 36-39, drawn to method of assaying genetic propensity of a patient to develop a disorder associated with epithelial barrier formation by assaying DNA or RNA, classified in class 435, subclass 6.

VII. Claims 40 and 41, drawn to protein of SEQ ID NO:9, classified in class 530, subclass 300.

VIII. Claims 40 and 41, drawn to protein of SEQ ID NO:10, classified in class 530, subclass 300.

IX. Claims 40 and 41, drawn to protein of SEQ ID NO:11, classified in class 530, subclass 300.

X. Claims 40 and 41, drawn to protein of SEQ ID NO:12, classified in class 530, subclass 300.

XI. Claim 42, drawn to method of retarding progression of a pre-malignant epithelial cell towards malignancy, classification dependent on structure of agonist, for example, classified in class 512, subclass 2.

XII. Claims 43-48, drawn to method of retarding progression of a skin cancer by administer an antagonist of the Notch pathway, classification dependent on structure of antagonist, for example, classified in class 512, subclass 2.

XIII. Claims 43, 45, 46 and 49, drawn to method of retarding progression of a skin cancer by administer an agonist of the Notch pathway, classification dependent on structure of agonist, for example, classified in class 512, subclass 2.

XIV. Claims 50-52, drawn to method of diagnosing aggressive melanoma by assaying biopsy for overexpression of a protein, classified in class 435, subclass 7.1.

XV. Claim 53, drawn to method of diagnosing CTCL by assaying biopsy for expression of a T-cell-specific marker and a Notch receptor and a Notch ligand, classified in class 435, subclass 7.21.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different modes of operation because they have distinct methods steps and actions necessary for intracellular *versus* extracellular application.

Inventions I and II are unrelated to Invention V. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different modes of operation and effects, so that while they might use the same active agent, the outcomes are sufficiently different to require a burdensome search. Inventions I and II do not require differentiation in culture nor into epidermis.

Inventions I and II are unrelated to each of Inventions III, IV, VI, XI-XV. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP §

808.01). In the instant case the different inventions have different effects, so that while they might use the same active agent, the outcomes are sufficiently different to require a burdensome search.

Inventions III and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different modes of operation because they have distinct methods steps and actions necessary for intracellular *versus* extracellular application.

Inventions III and IV are unrelated to Invention V. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different modes of operation and effects, so that while they might use the same active agent, the outcomes are sufficiently different to require a burdensome search. Inventions III and IV do not require culturing or the production of epidermis.

Each of Inventions III-IV, VI and XI-XV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different effects, so that while they might use the same active agent, the outcomes are sufficient different to require a burdensome search. Note Invention VI also has a different mode of operation, requiring a diagnostic nucleic acid instead of an agonist. Also, Inventions XIV and XV require assaying, but do not require the use of a Notch agonist in the assay. Invention XII requires the use of an antagonist, unlike the other methods.

Inventions VII-X are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different structures, and while some functions might overlap, the proteins are necessarily distinct, each requiring a different sequence search.

Inventions I-V, VII-X and XI are related as product and process of use to each of XIII-XV. The inventions can be shown to be distinct if either or both of the following can be shown:

(1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case none of the methods of I-V,XI and XIII-XV specifically requires the use of one of the proteins of VII-X, although the proteins are included in a Markush group for claim 24(IV). The proteins can be used in a materially different process such as in the production of antibodies for detection assays or in the identification of a binding partner for said proteins.

Each of Inventions VI and XII are unrelated to each of Inventions VII-X. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions cannot be used together, the methods require an antagonist or a nucleic acid.

Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification, have recognized divergent subject matter, and because each invention requires a separate non-coextensive search, restriction for examination purposes as indicated is proper.

This application contains claims directed to the following patentably distinct species of 1) **Notch agonists** of the claimed invention: Jagged-1, Jagged-2, Delta, Lunatic Fringe, Manic Fringe, Radical Fringe, Serrate, each one of SEQ ID NO:2-12, constitutively active Notch-1, -2, -3, and -4, and antisense; and 2) **Notch antagonists** of the claimed invention: gamma secretase inhibitor, SEQ ID NO:16 and 18 (claim 48); and 3) **biopsy protein**: JAG-1, JAG-2, Delta, Notch-1, Notch-2, Notch-3, Notch-4,CD31, CD43 and CD54 (claim 51). Note that if Applicant choose for the SEQ ID NO:2-12, if any one corresponds to one of the named proteins, Applicant should state this to ensure complete examination.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, for 1) claims 1-3, 14-19, 30-35, 42-46, 49, 50 and 53 are generic; for 2) claims 43-46; and for 3) claims 50 and 53. Note that each of the 3 species groups covers multiple Inventions. So once an Invention group is chosen, a species for that appropriate Invention must also be chosen.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (703) 305-5791. Dr. Kaufman can generally be reached Monday through Thursday from 8:30AM to 12:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (703) 308-6564.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. **Please** advise the examiner at the telephone number above before facsimile transmission.

Claire M. Kaufman, Ph.D.

Patent Examiner, Art Unit 1646

May 20, 2003